

Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims

1. (Currently Amended) A method of identifying a candidate therapeutic agent for use in the treatment of acute pancreatitis, the method comprising:

providing a cell expressing a TLR4 protein;

contacting the cell with a test compound; ~~and~~

~~evaluating performing an assay to measure an effect of the test compound on~~ an activity of the TLR4 protein in the presence of the test compound, and

selecting the test compound as a candidate agent for treating acute pancreatitis if the compound reduces the activity of the TLR4 protein.

~~wherein a test compound that reduces the activity of the TLR4 protein is a candidate therapeutic agent for use in the treatment of acute pancreatitis.~~

2. (Original) The method of claim 1, wherein the test compound reduces the activity of the TLR4 protein by reducing a level of TLR4 proteins.

3. (Original) The method of claim 2, wherein the test compound reduces the level of TLR4 proteins by reducing one or more of (i) transcription of TLR4 mRNA or (ii) half-life of TLR4 mRNA.

4. (Original) The method of claim 2, wherein the test compound reduces the level of TLR4 proteins by reducing one or more of (i) translation of TLR4 protein, (ii) trafficking of TLR4 protein, (iii) half-life of TLR4 protein, or (iv) cellular localization of TLR4 protein.

5. (Withdrawn) The method of claim 1, wherein the test compound reduces the activity of the TLR4 protein by interfering with binding of TLR4 to a TLR4 binding partner.

6. (Withdrawn) The method of claim 5, wherein the TLR4 binding partner is selected from the group consisting of Toll-interacting protein (Tollip), myeloid differentiation factor 88

(MyD88), TIR domain-containing adapter protein (TIRAP/MAL), MD-2, CD14, and IL-1R-associated kinase (IRAK).

7. (Withdrawn) The method of claim 1, wherein the test compound reduces the activity of the TLR4 protein by altering one or more post-translational modifications.

8. (Currently Amended) The method of claim 1, wherein the test compound is an siRNA, ~~antisense nucleic acid, ribozyme, or TLR4 specific antibody.~~

9. (Withdrawn) The method of claim 1, further comprising:
providing a model system for acute pancreatitis;
contacting the model system with a test compound that reduces an activity of the TLR4 protein; and
evaluating a clinical parameter relating to the acute pancreatitis in the model system in the presence and the absence of the test compound,
wherein an improvement in the clinical parameter indicates that the test compound is a candidate therapeutic agent for use in the treatment of acute pancreatitis.

10. (Withdrawn) A method of identifying a candidate therapeutic agent for use in the treatment of acute pancreatitis, the method comprising:
providing a test compound that is known or suspected to decrease TLR4 activity;
providing a model system for acute pancreatitis;
contacting the model system with the test compound; and
evaluating a clinical parameter relating to the acute pancreatitis in the model system in the presence and the absence of the test compound,
wherein an improvement in the clinical parameter indicates that the test compound is a candidate therapeutic agent for use in the treatment of acute pancreatitis.

11. (Withdrawn) The method of claim 9, wherein the model system is an animal model of acute pancreatitis.

12. (Withdrawn) The method of claim 11, wherein the parameter is measured by measuring myeloperoxidase (MPO) activity, serum amylase levels, percent necrosis, or percent edema in the pancreas of the animal model.

13. (Withdrawn) The method of claim 9, wherein the model system is a patient diagnosed with acute pancreatitis.

14. (Withdrawn) The method of claim 9, wherein the parameter relating to the acute pancreatitis is time of onset, severity, duration, or recurrence.

15. (Withdrawn) The method of claim 9, wherein the parameter relating to the acute pancreatitis is the presence of a pancreatitis-associated disorder selected from the group consisting of lung injury, kidney failure, and heart failure.

16. (Cancelled)

17. (Cancelled)

18. (Withdrawn) The method of claim 10, wherein the model system is an animal model of acute pancreatitis.

19. (Withdrawn) The method of claim 18, wherein the parameter is measured by measuring myeloperoxidase (MPO) activity, serum amylase levels, percent necrosis, or percent edema in the pancreas of the animal model.

20. (Withdrawn) The method of claim 10, wherein the model system is a patient diagnosed with acute pancreatitis.

21. (Withdrawn) The method of claim 10, wherein the parameter relating to the acute pancreatitis is time of onset, severity, duration, or recurrence.

22. (Withdrawn) The method of claim 10, wherein the parameter relating to the acute pancreatitis is the presence of a pancreatitis-associated disorder selected from the group consisting of lung injury, kidney failure, and heart failure.

23. (Cancelled)

24. (Cancelled)

25. (New) The method of claim 1, wherein the test compound is a small molecule.

26. (New) The method of claim 1, wherein the test compound is an antisense nucleic acid.

28. (New) The method of claim 1, wherein the test compound is a ribozyme.

29. (New) The method of claim 1, wherein the test compound is a TLR4-specific antibody.